UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/937,519	03/05/2002	Guido Krupp	P-UX 4977	9641

41552 7590 05/01/2006

MCDERMOTT, WILL & EMERY
4370 LA JOLLA VILLAGE DRIVE, SUITE 700
SAN DIEGO, CA 92122

EXAMINER	
STRZELECKA, TERESA E	

ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 05/01/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/937,519	KRUPP, GUIDO	
	Examiner	Art Unit	
	Teresa E. Strzelecka	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 September 2005 and 06 February 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,5-11 and 30-72* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,5-11 and 30-72* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *2/6/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. This office action is in response to amendments filed September 12, 2005 and February 6, 2006. Claims 1-29 were previously pending, with claims 2, 4 and 12-29 withdrawn from consideration. Applicant cancelled claims 2, 4 and 12-29, amended claims 1, 3, 6-9 and 11 and added new claims 30-72. Claims 1, 3, 5-11 and 30-72 are pending and will be examined.

2. Applicant's amendments to the claims overcame the following: objections to claims 1, 3 and 5-11; rejection of claims 1, 3 and 5 under 35 U.S.C. 112, second paragraph. All other rejections are maintained for reasons given in the "Response to Arguments" below.

3. Applicant's submission of a sequence listing and amendments to the specification put the application in compliance with sequence rules required by 37 C.F.R. 1.821-1.825.

Information Disclosure Statement

4. The information disclosure statement (IDS) submitted on February 6, 2006 was filed after the mailing date of the non-final office action on March 11, 2005. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner. Reference AN1 was not considered, since it is a duplicate of a reference filed in a previous IDS.

Response to Arguments

5. Applicant's arguments filed September 12, 2005 and February 6, 2006 have been fully considered but they are not persuasive.

Regarding the rejection of claims 1, 3 and 5 under 35 U.S.C. 103(a) over Uijtewaal et al. (EPO 0 416 572 A1), Leone et al. (Nucl. Acids Res., vol. 26, pp. 2150-2155, 1998) and Heid et al. (Genome Research, vol. 6, p. 986-994, 1996), Applicant argues that the references do not teach or suggest the claim invention, without providing reasons why it is so.

The rejection is maintained in a form encompassing claims which were previously not examined on the merits and the newly added claims.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 6, 8, 10, 30-35, 37, 39, 41, 43, 46, 48, 51, 53, 55, 58, 60, 62, 64, 67 and 69 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claims, 6 and 51 are indefinite over the recitation of "the nucleic acid sequence attached to the primer has a length of 1 to 40 nucleotides". However, claim 1, from which these claims depend, requires that the attached sequence be 5'-GAAA-3', therefore the attached sequence has to have at least four nucleotides.

B) Claims 8, 32, 37, 41, 53, 58 and 62 are indefinite over the recitation of "the nucleic acid probe has a length of 25 to 60 nucleotides preferably approx. 50 nucleotides". It is therefore not clear whether the claimed length of the probe is 25-60 nucleotides or 50 nucleotides.

C) Claims 10, 34, 39, 43, 46, 48, 55, 60, 64, 67 and 69 are indefinite over the use of trademark name. Claim 10, 34, 39, 43, 46, 48, 55, 60, 64, 67 and 69 contain the trademark/trade name NASBA®. Where a trademark or trade name is used in a claim as a limitation to identify or describe a particular material or product, the claim does not comply with the requirements of 35 U.S.C. 112, second paragraph. See *Ex parte Simpson*, 218 USPQ 1020 (Bd. App. 1982). The claim scope is uncertain since the trademark or trade name cannot be used properly to identify any particular material or product. A trademark or trade name is used to identify a source of goods, and not the goods themselves. Thus, a trademark or trade name does not identify or describe the goods

associated with the trademark or trade name. In the present case, the trademark/trade name is used to identify/describe a method and, accordingly, the identification/description is indefinite.

D) Claims 30-35 are indefinite in claim 30. Claim 30 is indefinite over the recitation of "the nucleic acid sequence attached to the primer has a length of 1 to 40 nucleotides". However, claim 3, from which claim 30 depends, does not contain a limitation of a sequence attached to a primer.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claims 1, 3, 5-11 and 30-72 are rejected under 35 U.S.C. 103(a) as being unpatentable over Uijtewaal et al. (EPO 0 416 572 A1; cited in the previous office action), Leone et al. (Nucl. Acids Res., vol. 26, pp. 2150-2155, 1998; cited in the previous office action) and Heid et al. (Genome Research, vol. 6, p. 986-994, 1996; cited in the previous office action).

A) Regarding claims 1 and 3, Uijtewaal et al. teach construction of ribozyme-encoding oligonucleotides with sequences complementary to sequences of plant proteins, such as polygalcouronase, pectin esterase and ripening related protein. The ribozymes contained sequence motifs 5'-GAAA-3' and 5'-CTGATGA-3', which, after expression in plants, produced a motif of 5'-CUGAUGA-3' (page 3, lines 28-58; page 4, lines 47-58; page 5, lines 1-16; page 8, lines 1-44).

Uijtewaal et al. teach transformation of ribozyme-encoding vectors into tomato plants and detection of the ribozyme sequences by hybridization of the oligonucleotides containing the 5'-CTGATGA-3'motif with total RNA isolated from transgenic plants (page 6, lines 18-58; page 7, lines 1-29).

Regarding claims 5 and 72, Uijtewaal et al. teach RNA (page 8, lines 23-44).

Regarding claims 6, 30 and 51, Uijtewaal et al. teach a GAAA motif (page 5, lines 1-16; page 8, lines 1-44), therefore they teach 4 nucleotides.

Regarding claims 8, 32, 37, 41, 53, 58 and 62, Uijtewaal et al. teach oligonucleotide probes having a length of 48 nucleotides (page 5, lines 1-16; page 8, lines 1-44).

B) Uijtewaal et al. do not teach real-time detection of the ribozymes using a probe labeled with a reporter and a quencher.

C) Regarding claims 1 and 3, Leone et al. teach detection of RNA of potato leaf roll virus (PLRV) in potato tubers using real-time NASBBA amplification reaction with a probe containing a reporter molecule and a quencher molecule (Abstract; page 2151, paragraphs 3-5 and 10; page 2152, first paragraph). Leone et al. teach determination of the different amounts of the PLRV in the samples using real-time NASBA (page 2153, last two paragraphs; page 2154, first and second paragraph; Fig. 3 and 7).

Regarding claims 9, 10, 33, 34, 38, 39, 42, 43, 45, 46, 48, 54, 55, 59, 60, 63, 64, 66, 67 and 69, Leone et al. teach isothermal NASBA amplification (page 2150, first paragraph).

D) Leone et al. do not teach determination of the original concentration of nucleic acids using the threshold values for the sample and reference.

E) Regarding claims 1 and 3, Heid et al. teach real time quantitative PCR (Abstract), in which the threshold value C_T, equal to a number of amplification cycles, and, therefore, time, after

which the fluorescence becomes detectable, is related to the number of nucleic acid molecules in the reaction (Fig. 1; page 988; page 989, first paragraph). The relationship between C_T values and the amount of input target sequences is quantitative (page 989, second paragraph; Fig. 1B and C). Therefore, the amount of initial target nucleic acid can be determined using a reference sample (internal control) for quantitation (page 990; page 991, paragraphs 1-3; Fig. 4).

Regarding claims 7, 31, 36, 52 and 57, Heid et al. teach concentrations of molecular beacons of 100 nM (page 993, third paragraph).

Regarding claims 11, 35, 40, 44, 47, 49, 50, 56, 61, 65, 68, 70 and 71, Heid et al. teach FAM and TAMRA (page 987, third and fourth paragraph).

It would have been *prima facie* obvious to one of ordinary skill in the art to have used the real-time detection methods of Leone et al. and Heid et al. to detect ribozymes in transfected plants of Uijtewaal et al. The motivation to do so, as provided by Leone et al., would have been that (page 2155, last paragraph):

> "... the novel technology presented in this report offers a truly homogeneous assay in which amplification and detection of RNA occur in one-tube. Compared to current RNA probing and/or blotting methods, the use of molecular beacons to detect NASBA amplicons, retains the same level of specificity and sensitivity, is easy to perform and timesaving, due to a reduction of handling steps. The risk of carry-over contamination is minimized by the advantage of performing the entire method in unopened vessels. Furthermore the assay is sensitive and robust, as demonstrated by working with very complex samples such as potato tuber extracts. This shows that AmpliDet RNA has the potential to be used in routine settings for high-throughput sample analysis."

The motivation to do so, provided by Heid et al., would have been that, as stated be Heid et al. (page 992, first and second paragraphs):

"Second, this method supports the use of normalization gene (i.e., β-actin) for quantitative PCR or housekeeping genes for quantitative RT-PCR controls. Analysis is performed in real time during the log phase of product accumulation. Analysis during log phase permits many different genes (over a wide input target range) to be analyzed simultaneously, without concern of reaching reaction plateau at different cycles. This will make multigene analysis much easier to develop, because individual internal competitors will not be needed for each gene under analysis. Third, sample throughput will increase dramatically with the new method because there is no post-PCR processing time. ... The real-time PCR method is highly reproducible. Replicate amplifications can be analyzed for each sample minimizing potential error. The system allows for a very large assay dynamic range (approaching 1,000,000-fold starting target). Using a standard curve for the target of interest, relative copy number values can be determined for any unknown sample."

10. No claims are allowed.

Conclusion

11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Teresa E. Strzelecka whose telephone number is (571) 272-0789. The examiner can normally be reached on M-F (8:30-5:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Teresa E Strzelecka
Primary Examiner
Art Unit 1637
Teresa Strzelecka
4/28/06